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APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A
FILING DATE.

APPLICATION NUMBER: 60/405,352

FILING DATE: August 23, 2002

RELATED PCT APPLICATION NUMBER: PCT/US03/26238



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COMMISSIONER OF PATENTS AND TRADEMARKS

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Approved for use through 10/31/2002. OMB 0651-0032

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No.

1996 U.S. P.T.O. 405352

INVENTOR(S)					
Given Name (first and middle (if any))		Family Name or Surname		Residence (City and either State or Foreign Country)	
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<input type="checkbox"/> Additional inventors are being named on the _____ separately numbered sheets attached hereto					
TITLE OF THE INVENTION (500 characters max)					
Methods and apparatus for non-invasively evaluating endothelial function					
Direct all correspondence to: CORRESPONDENCE ADDRESS					
<input type="checkbox"/> Customer Number		<input type="text"/>		<input type="text"/>	
OR		Type Customer Number here		Place Customer Number Bar Code Label here	
<input type="checkbox"/> Firm or Individual Name		Morteza Naghavi			
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Address					
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Country		USA	Telephone	832-355-9144	Fax 832-355-9368
ENCLOSED APPLICATION PARTS (check all that apply)					
<input checked="" type="checkbox"/> Specification		Number of Pages 5		<input type="checkbox"/> CD(s), Number <input type="text"/>	
<input checked="" type="checkbox"/> Drawing(s)		Number of Sheets 1		<input checked="" type="checkbox"/> Other (specify) references	
<input type="checkbox"/> Application Data Sheet. See 37 CFR 1.76					
METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT					
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27.				FILING FEE AMOUNT (\$)	
<input checked="" type="checkbox"/> A check or money order is enclosed to cover the filing fees				\$80.00	
<input type="checkbox"/> The Commissioner is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: <input type="text"/>					
<input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.					
The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.					
<input checked="" type="checkbox"/> No					
<input type="checkbox"/> Yes, the name of the U.S. Government agency and the Government contract number are: _____					

Respectfully submitted,

SIGNATURE

Date

08/21/2002

TYPED or PRINTED NAME

Morteza Naghavi

REGISTRATION NO.

(If appropriate)
Docket Number:

TELEPHONE

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is used by the public to file (and by the PTO to process) a provisional application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the complete provisional application to the PTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Box Provisional Application, Assistant Commissioner for Patents, Washington, D.C. 20231.

61405357.082342

PTO/SB/17 (10-01)

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**FEE TRANSMITTAL
for FY 2002**

Patent fees are subject to annual revision.

Complete if Known

Application Number	
Filing Date	08/21/2002
First Named Inventor	Morteza Naghavi, MD
Examiner Name	
Group Art Unit	
Attorney Docket No.	

TOTAL AMOUNT OF PAYMENT (\$) 80.00**METHOD OF PAYMENT**

- 1.
- ☐
- The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

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- ☐
- Applicant claims small entity status See 37 CFR 1.27

- 2.
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Large Entity Code	Small Entity Code	Fee (\$)	Fee (\$)	Fee Description	Fee Paid
101	740	201	370	Utility filing fee	
106	330	206	165	Design filing fee	
107	510	207	255	Plant filing fee	
108	740	208	370	Reissue filing fee	
114	160	214	80	Provisional filing fee	

SUBTOTAL (1) (\$) 80.00**2. EXTRA CLAIM FEES**

Total Claims	Extra Claims	Fee from below	Fee Paid
Independent	-20** =	X	
Multiple Dependent	-3** =	X	

Large Entity Code	Small Entity Code	Fee (\$)	Fee (\$)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claim, if not paid
109	84	209	42	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) (\$)

**or number previously paid, if greater, For Reissues, see above

FEE CALCULATION (continued)**3. ADDITIONAL FEES**

Large Entity Fee Code	Small Entity Fee Code	Fee (\$)	Fee (\$)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for ex parte reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
116	110	215	55	Extension for reply within first month	
118	400	216	200	Extension for reply within second month	
117	920	217	460	Extension for reply within third month	
118	1,440	218	720	Extension for reply within fourth month	
128	1,960	228	980	Extension for reply within fifth month	
119	320	219	160	Notice of Appeal	
120	320	220	160	Filing a brief in support of an appeal	
121	280	221	140	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,280	241	640	Petition to revive - unintentional	
142	1,280	242	640	Utility issue fee (or reissue)	
143	460	243	230	Design issue fee	
144	620	244	310	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1.17(q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	740	246	370	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	740	249	370	For each additional invention to be examined (37 CFR § 1.129(b))	
179	740	279	370	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify)

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) (\$)**SUBMITTED BY**

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(Attorney/Agent)

Complete if applicable

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Signature

Date

08/21/2002

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Title: - Methods and apparatus for non-invasively evaluating endothelial function.

Inventors: Nachiket Kharalkar
Dr. Morteza Naghavi

Endothelial dysfunction in cardiovascular diseases,
http://www.atmedica.com.sg/disppdf.cfm?fname=MP_May2002_CVD.pdf,
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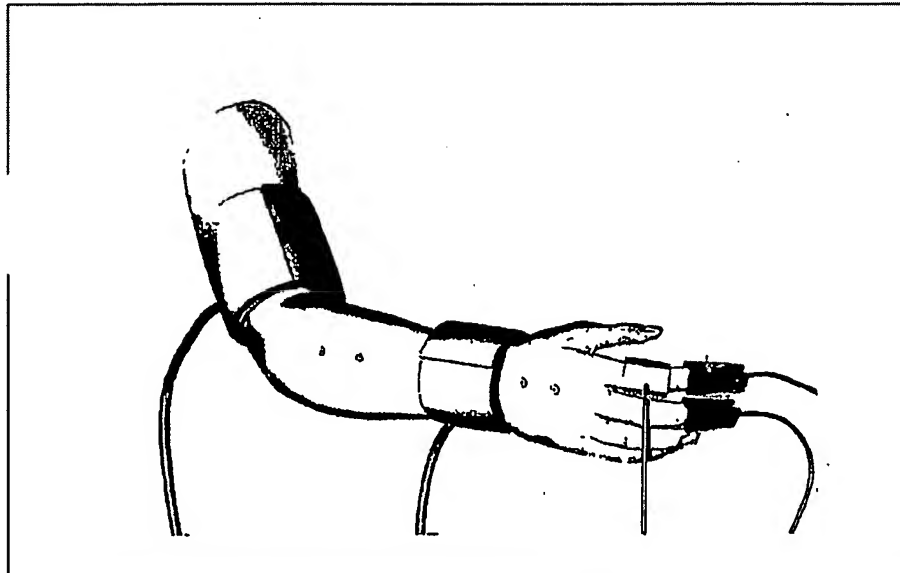
ABSTRACT

Methods and apparatus for non-invasively evaluating endothelial function. This can be done self-administratively without the presence of any medical practitioner. This test helps an ordinary consumer or patient to test the endothelial function and to obtain information about his endothelial cells; which are responsible for maintaining the patency

and integrity of the arterial system. The hyperemia is simulated by creating an occlusion of the target artery (by inducing cuff pressure on arm, wrist, finger or leg) for some time and then suddenly releasing the occlusion. The changes in the arterial blood flow are monitored before the occlusion and then after the release of occlusion. Different techniques may be used to determine the blood flow through the arteries and may include but are not limited to pulse oximetry, temperature measurements, piezoelectric sensors or auditory sensors. These changes are then used to predict the endothelium dysfunction present if any.

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[0030]

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Figure 4



Methods and apparatus for non-invasively evaluating endothelial function

FIELD OF THE INVENTION

The present invention relates generally to evaluation of the endothelial function. More particularly, it allows medical examination of the vascular system, in the absence of the medical practitioner, at the public places such as shopping complex, airport, mall etc.

BACKGROUND OF THE INVENTION

Over the past two- three decades, the ability to diagnose heart disease has improved radically. This is primarily because of the evolution of new, increasingly sophisticated cardiac-testing techniques and equipments. Cardiovascular diseases and its sequel account for most of the morbidity and mortality in advanced countries. Although the exact cause of cardiovascular disease remains ambiguous, it is now known that an impairment of tissue perfusion represents the primary problem. The understanding of the development and progression of atherosclerosis has been greatly advanced in the past decade. In 1970's the response to injury hypothesis of atherosclerosis proposal was made; suggesting atherosclerosis begins with an injury to the arterial wall leading to endothelial denudation or 'stripping of the endothelial lining of the artery'. In recent years, it has become clear that the endothelium has many important functions in maintaining the patency and integrity of the arterial system. The endothelium can reduce and so inactivate toxic super-oxides which may be present in diabetics and in smokers. The endothelium is the source of the nitric oxide, a local hormone that relaxes the adjacent smooth muscle cells in the media, and is one of the most powerful vasodilators known. The endothelium regulates vascular homeostasis by elaborating a variety of paracrine factors that act locally in the blood vessel wall and lumen. Under normal conditions, the sum total effect of these endothelial factors is to maintain normal vascular tone, blood fluidity, and limit vascular inflammation and smooth muscle cell proliferation. However, when coronary risk factors are present, the endothelium may adopt a phenotype that facilitates inflammation, thrombosis, vasoconstriction, and atherosclerotic lesion formation. In human subjects, this maladaptive endothelial phenotype manifests itself prior to the development of frank atherosclerosis and is associated with traditional risk factors such as hypercholesterolemia, hypertension, and diabetes

mellitus and with emerging risk factors such as hyperhomocystinemia, obesity, and systemic inflammation.

Possible causes of endothelial dysfunction include:-

- Elevated low density lipoprotein cholesterol, particularly oxidized LDL-C.
- Free radical induced damage caused by tobacco use, diabetes and hypertension.
- Genetic abnormalities.
- Elevated plasma homocysteine.
- Infectious agents such as Chlamydia.
- Obesity.
- Sedentary lifestyle.

Currently available methods for the estimation of the endothelial dysfunction can be classified in to two types; invasive and non-invasive methods.

Invasive methods are:-

1. Coronary endothelial function is frequently studied by measuring the vasodilator response of coronary arteries to acetylcholine or to cold pressor test by invasive quantitative coronary angiography.
2. Injecting the radioactive material, and then tracing the blood flow with the help of gamma ray radiations.

add to [0007]

Non-invasive methods are:-

1. Method to evaluate the accuracy of measurement of the percent change in diameter of the left main trunk induced by cold pressor test with two-dimensional (2-D) echocardiography and extension of this method to the evaluation of coronary artery endothelial function in hypertensive patients.
2. Dundee step test.
3. Laser Doppler perfusion imaging and iontophoresis (Linton instruments).
4. High resolution B-mode ultrasound.
5. Detection of vascular conditions using an occlusive arm cuff plethysmograph.
6. Detection of medical conditions by monitoring the peripheral arterial tone, in conjunction with the creation of hyperemia by the arm cuff.

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SUMMARY OF THE INVENTION

This Invention introduces a self administered endothelial function assessment test. The test is a non-invasive test for evaluation of endothelial function and can be done without the presence of any medical practitioner. The main endeavor for developing these tests is to enable an ordinary consumer or patient to test their endothelial function and get the information about his endothelial cells; which are responsible for maintaining the patency and integrity of the arterial system. In a self administered fashion this endothelial function assessment kit can be made available in the Check-my heart café, various public places, and also can be made home based.

This invention helps us in predicting the endothelial dysfunction non-invasively, without the presence of any medical practitioner. Currently available methods require the presence of skilled medical practitioner. These self administered endothelial function assessment tests can be performed at the public places and also at the home. The hospital based tests currently available are costly. The tests mentioned in this invention can be performed in 5-6 minutes. Currently available tests may sometimes require more than 6 minutes for the test.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is an overall system diagram of the invention, in its preferred embodiment.

We claim:

1. A self administered method for non-invasive detection of the endothelial function of a person, without the intervention of any medical practitioner.

2. A method for self administered endothelial function evaluation comprising:

Creation of occlusion on the arm, leg, wrist or finger of a person in order to block the arterial blood flow;

Maintaining of the said occlusion for predetermined time at the predetermined pressure;

Removing the occlusion after predetermined period;

Monitoring of the changes in the oxygen content of the blood, temperature of finger tip or the blood flow rate;

Prediction of the EF from the analysis of above parameters.

3. A method as mentioned in claim (2), wherein the pulse oximeter is connected to the tip of finger to continuously monitor the oxygen content of the blood in order to predict the EF.

4. A method as mentioned in claim (2), wherein the temperature sensors are placed on the tip of the finger, to monitor the blood flow and predict the EF from that.

5. A method as mentioned in claim (2), wherein two or more sensors separated by some known distance are placed on the forearm of the person when the occlusion is created in the arm, to determine the blood flow rate. The sensors may be piezo electric sensors, micro phone, pressure etc.

6. A method as mentioned in claim (2), wherein Photoplethysmograph apparatus is placed near the finger to monitor the blood flow.

7. A method as mentioned in claim (2), wherein two or more sensors separated by some distance are placed on the arm or the hand and the impedance between them is continuously monitored. This in turn gives the endothelial function.

8. A method as mentioned in claim (2), wherein the blood flow is measured with the help of MARENIR technique.

9. A method as mentioned in claim (2), wherein the blood flow and the changes in the artery dimensions are monitored by the combined Ultrasound-Doppler technique.

10. A method as mentioned in claim (2), which monitors the blood flow over the course of time right from before the creation of

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occlusion till the blood flow is normalized after the removal of the occlusion, in order to exactly predict the Endothelial function.

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11. A method as mentioned in claim (2), wherein the blood flow and the change in the blood flow are plotted against the time. These two graphs are further analyzed to give more accurate value of the endothelial function.

12. The self-administer endothelial function assessment system as mentioned in claim (1), which gives the 'Risk factor score' to the patient at the end of the test; indicating the amount of risk the user has.

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[0035]

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